Atty Dkt 8325-0002.01 **PATENT**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on 14 Nov 2001

#9

1-17-11

Susan La Mont

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

G.N. Cox III et al.

Serial No.: 09/897,844

Group Art Unit: 1631

Filing Date: July 2, 2001

Examiner: Unassigned

Title:

REGULATION OF ENDOGENOUS GENE EXPRESSION IN CELLS USING

ZINC FINGER PROTEIN

TRANSMITTAL LETTER

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

Transmitted herewith for filing is an Information Disclosure Statement and a Form PTO-1449. It is believed that no fee is due.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648.

Respectfully submitted,

Date: Nov 14, 2001

Dahna S. Pasternak Registration No. 41,411

ROBINS & PASTERNAK LLP 90 Middlefield Road, Suite 200 Menlo Park, CA 94025 Telephone: (650) 325-7812

Facsimile: (650) 325-7823

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

1 1 1 1

G.N. Cox III et al.

Serial No.: 09/897,844

Filing Date: July 2, 2001

Group Art Unit: 1631

Examiner: Unassigned

Title: REGULATION OF ENDOGENOUS GENE EXPRESSION IN CELLS USING ZINC

FINGER PROTEINS

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

The information listed below may be material to the examination of the above-identified application. A completed Form PTO-1449 listing the references identified below accompanies this paper.

All references are of record, or have been submitted in related application serial number 09/229,037 from which the present application claims priority under 35 U.S.C. §120. Thus, pursuant to C.F.R. §1.98(d), copies of the references are not included.

Applicants would appreciate the Examiner's initialing and returning the form to indicate that the references have been reviewed and made of record in the present application. The information includes:

United States Patent No. 4,990,607 issued February 5, 19919 to Katagiri et al.;

United States Patent No. 5,096,814 issued March 17, 1992 to Aivasidis et al.;

United States Patent No. 5,096,815 issued March 17, 1992 to Ladner et al.;

United States Patent No. 5,198,346 issued March 30, 1993 to Ladner et al.;

United States Patent No. 5,223,409 issued June 29, 1993 to Ladner et al.;

United States Patent No. 5,243,041 issued September 7, 1993 to Fernadez-Pol;

United States Patent No. 5,302,519 issued April 12, 1994 to Blackwood et al.;

United States Patent No. 5,324,638 issued June 28, 1994 to Tao et al.;

United States Patent No. 5,324,818 issued June 28, 1994 to Nabel et al.; United States Patent No. 5,324,819 issued June 28, 1994 to Oppermann et al.; United States Patent No. 5,340,739 issued August 23, 1994 to Stevens et al.; United States Patent No. 5,348,864 issued September 20, 1994 to Barbacid et al.; United States Patent No. 5,350,840 issued September 27, 1994 to Call et al.; United States Patent No. 5,356,802 issued October 18, 1994 to Chandrasegaran; United States Patent No. 5,376,530 issued December 27, 1994 to De The et al.; United States Patent No. 5,403,484 issued April 4, 1995 to Ladner et al.; United States Patent No. 5,436,150 issued July 25, 1995 to Chandrasegaran; United States Patent No. 5,487,994 issued January 30, 1996 to Chandrasegaran; United States Patent No. 5,498,530 issued March 12, 1996 to Schatz et al.; United States Patent No. 5,578,483 issued November 26, 1996 to Evans et al.; United States Patent No. 5,597,693 issued January 28, 1997 to Evans et al.; United States Patent No. 5,639,592 issued June 17, 1997 to Abramson et al.; United States Patent No. 5,674,738 issued October 7, 1997 to Abramson et al.; United States Patent No. 5,702,914 issued December 30, 1997 to Evans et al.; United States Patent No. 5,789,538 issued August 4, 1998 to Rebar et al.; United States Patent No. 5,792,640 issued August 11, 1998 to Chandrasegaran; United States Patent No. 5,869,618 issued February 9, 1999 to Lippman et al.; United States Patent No. 5,871,902 issued February 16, 1999 to Weininger et al.; United States Patent No. 5,871,907 issued February 16, 1999 to Winter et al.; United States Patent No. 5,916,794 issued June 29, 1999 to Chandrasegaran; United States Patent No. 5,939,538 issued August 17, 1999 to Leavitt et al.; United States Patent No. 5,972,615 issued October 26, 1999 to An et al.; United States Patent No. 6,001,885 issued December 14, 1999 to Vega et al.; United States Patent No. 6,007,988 issued December 28, 1999 to Choo et al.; United States Patent No. 6,013,453 issued January 11, 2000 to Choo et al.; International Publication No. WO 95 19431 published July 20, 1995; International Publication No. WO 95/06110 published February 29, 1996; International Publication No. WO 95/06166 published February 29, 1996;

Atty Dkt No. 8325-0002.01 USSN: 09/897,844

PATENT

International Publication No. WO 96/11267 published April 18, 1996;

International Publication No. WO 96/20951 published July 11, 1996;

International Publication No. WO 96/32475 published October 17, 1996;

International Publication No. WO 97/27212 published July 31, 1997;

International Publication No. WO 97/27213 published July 31, 1997;

International Publication No. WO 98/53057 published November 26, 1998;

International Publication No. WO 98/53058 published November 26, 1998;

International Publication No. WO 98/53059 published November 26, 1998;

International Publication No. WO 98/53060 published November 26, 1998;

International Publication No. WO 98/54311 published December 3, 1998;

International Publication No. WO 99/36553 published July 22, 1999;

International Publication No. WO 99/41371 published August 19, 1999;

International Publication No. WO 99/42474 published August 26, 1999;

International Publication No. WO 99/45132 published September 10, 1999;

International Publication No. WO 99/47656 published September 23, 1999;

International Publication No. WO 99/48909 published September 30, 1999;

International Publication No. WO 00/23464 published April 27, 2000;

International Publication No. WO 00/27878 published May 18, 2000;

European Publication No. O 873 567 A2 published April 8, 1998;

Agarwal et al., "Stimulation of Transcript Elongation Requires Both the Zinc Finger and RNA Polymerase II Binding Domains of Human TFIIS," *Biochemistry* 30(64):7842-7851 (1991);

Antao et al., "A Thermodynamic Study of Unusually Stable RNA and DNA Hairpins," *Nuc. Acids. Res.* 19(21):5901-5905 (1991);

Barbas, C. F., "Recent Advances in Phage Display," Curr. Opin. Biotech. 4:526-530 (1993);

Barbas et al., "Assembly of Combinatorial Antibody Libraries on Phage Surfaces: The Gene III Site," *PNAS* 88:7978-7982 (1991);

Barbas et al., "Semisynthetic Combinatorial Antibody Libraries: A Chemical Solution to the Diversity Problem," *PNAS* 89:4457-4461 (1992);

Beerli et al., "Toward Controlling Gene Expression at Will: Specific Regulation of the erbB-2/HER-2 Promoter by Using Polydactyl Zinc Finger Proteins Constructed From Modular Building Blocks," *Proc. Natl. Acad. Sci. U.S.A.* <u>95</u>:14628-14633 (1998);

g - 1 - 2 - 2

Bellefroid et al., "Clustered Organization of Homologous KRAB Zinc-Finger Genes With Enhanced Expression in Human T Lymphoid Cells," *EMBO J.* 12(4):1363-1374 (1993); Berg, J.M., "DNA Binding Specificity of Steroid Receptors," *Cell* 57:1065-1068 (1989); Berg, J.M., "Sp1 and the Subfamily of Zinc-Finger Proteins with Guanine-Rich Binding Sites," *PNAS* 89:11109-11110 (1992);

Berg et al., "The Galvanization of Biology: A Growing Appreciation for the Roles of Zinc," Science 271:1081-1085 (1996);

Berg, J.M., "Letting Your Fingers do the Walking," *Nature Biotechnology* <u>15</u>:323 (1997);

Bergqvist et al., "Loss of DNA-binding and new Transcriptional Trans-Activation Function in Polyomavirus Large T-Antigen with Mutation of Zinc Finger Motif," *Nuc. Acids Res.* 18(9):2715-2720 (1990);

Blaese et al., "Vectors in Cancer Therapy: How Will They Deliver?," Cancer Gene Therapy 2(4):291-297 (1995);

Caponigro et al., "Transdominant Genetic Analysis of a Growth Control Pathway," PN.AS 95:7508-7513 (1998);

Celenza et al., "A Yeast Gene That Is Essential for Release from Glucose Repression Encodes a Protein Kinase," *Science* 233:1175-1180 (1986);

Cheng et al., "Identification of Potential Target Genes for Adrlp through Characterization of Essential Nucleotides in UASI," *J. Mol. Cellular Biol.* <u>14</u>(6):3842-3852 (1994);

Cheng et al., "A Single Amino Acid Substitution in Zinc Finger 2 of Adrlp Changes its Binding Specificity at two Positions in UAS1," J. Mol. Biol. 251:1-8 (1995);

Choo et al., "A Role in DNA-Binding for the Linker Sequences of the First Three Zinc Fingers of TFIIIA *Nuc. Acids Res.* 21(15):3341-3346 (1995);

Choo et al., "Designing DNA-Binding Proteins on the Surface of Filamentous Phage," Curr. Opin. Biotechnology 6:431-436 (1995);

Choo et al., "Promoter-Specific Activation of Gene Expression Directed By Bacteriophage-Selected Zinc Fingers," *J. Mol. Biol.* 273:525-532 (1997);

, , ,

Choo, Y., "Recognnition of DNA Methylation by Zinc Fingers," *Nature Struct Biol.* 5(4):264-365 (1998);

Choo et al., "All Wrapped Up," Nature Structural Biology 5(4):253-255 (1998);

Choo, Y., "End Effects in DNA Recognition Code," Nuc. Acids. Res. 26(2):554-557 (1998);

Choo et al., Physical Basis of Protein-DNA Recognition Code," Curr. Opin. Struct. Biol. 7(1):117-125 (1997);

Choo et al., "In Vivo Expression by a Site-Specific DNA-Binding Protein Designed Against an Oncogenic Sequence," *Nature* 372:642-645 (1994);

Choo et al., "Selection of DNA Binding Sites for Zinc Fingers Using Rationally Randomized DNA Reveals Coded Interactions," *Proc. Natl. Acad. Sci. U.S.A.* 91:11168-11172 (1994);

Choo et al., "Toward a Code for the Interactions of Zinc Fingers With DNA: Selection of Randomized Fingers Displayed on Phage," *Proc. Natl. Acad. Sci. U.S.A.* 91:11163-11167 (1994);

Clark et al., "Zinc Fingers in Caenorhabditis elegans: Finding Families and Probing Pathways," Science 282:2018-2022 (1998);

Corbi et al., "Synthesis of a New Zinc Finger Peptide: Comparison of Its "Cod" Deduced and CASTing Derived Binding Sites," *FEBS Letters* 417:71-74 (1997);

Crozatier et al., "Single Amino Acid Exchanges in Separate Domains of the Drosophila Serendipity δ Zinc Finger Protein Cause Embroyonic and Sex Biased Lethality," *Genetics* 131:905-916 (1992);

Debs et al., Regulation of Gene Expression in Vivo by Liposome-Mediated Delivery of a Purified Transcription Factor," J. Biological Chemistry 265(18):10189-10192 (1990);

Desjarlais et al., "Redesigning the DNA-Binding Specificity of a Zinc Finger Protein: A Data Base-Guided Approach," *Proteins: Structure, Function, and Genetics* 12(2):101-104 (1992); Desjarlais et al., "Redesigning the DNA-Binding Specificity of a Zinc Finger Protein: A

Data Base-Guided Approach," Proteins: Structure, Function, and Genetics 12(2):101-104 (1992);

Desjarlais et al., "Redesigning the DNA-Binding Specificity of a Zinc Finger Protein: A Data Base-Guided Approach," *Proteins: Structure, Function, and Genetics* 13(3):272 (1992);

Desjarlais, J. R. and Berg, J.M., "Length-Encoded Multiplex binding Site Determination:

Application to Zinc Finger Proteins," Proc. Natl. Acad. Sci. U.S.A. 91:11099-11103 (1994);

Desjarlais, J. R. and Berg, J.M., "Use of a Zinc-Finger Consensus Sequence Framework and Specificity Rules to Design Specific DNA Binding Proteins," *Proc. Natl. Acad. Sci. U.S.A.* 90:2256-2260 (1993);

Desjarlais, J. R. and Berg, J.M., "Toward Rules Relating Zinc Finger Protein-Sequences and DNA Binding Preferences," *Proc. Natl. Acad. Sci. U.S.A.* <u>90</u>:7345-4349 (1992);

Dibello et al., "The Drosophila *Broad-Complex* Encodes a Family of Related Proteins Containing Zinc Fingers," *Genetics* 129:385-397 (1991);

Elrod-Erickson et al., "High-Resolution Structures of Variant Zif268-DNA Complexes:

Implications for Understanding Zinc Finger-DNA Recognition," Structure 6(4):451-464 (1998); Elrod-Erickson et al., "Zif268 Protein-DNA Complex Refined at 1.6 Å: a Model System for Understanding Zinc Finger-DNA Interactions," Structure 4(10):1171-1180 (1996);

Fairall et al., "The Crystal Structure of a Two Zinc-Finger Peptide Reveals an Extension to the Rules for Zinc-Finger /DNA Recognition," *Nature* 366:483-487 (1993);

Frankel et al., "Fingering Too Many Proteins," Cell 53:675 (1988);

Friesen et al., "Phage Display of RNA Binding Zinc Fingers from Transcription Factor IIA*," J. Biological Chem. 272(17):10994-10997 (1997);

Friesen et al., "Specific RNA Binding Proteins Constructed from Zinc Fingers," *Nature Structural Biology Biology* 5(7):543-546 (1998);

Gillemans et al., "Altered DNA binding Specificity Mutants of EKLF and Spl Show that EKLF is an Activator of the b-Globin Locus Control Region *in vivo*," *Genes and Development* 12:2863-2873 (1998);

Gogos et al., "Recognition of Diverse Sequences by Class I Zinc Fingers: Asymmetries and Indirect Effects on Specificity in the Interaction Between CF2II and A+T-Rich Sequences Elements," *PNAS* 93(5):2159-2164 (1996);

Gossen et al., "Tight Control of Gene Expression in Mammalian Cells by Tetracycline-Responsive Promoter," *PNAS* 89:5547-5551 (1992);

Greisman & Pabo, "A General Strategy for Selecting High-Affinity Zinc Finger Proteins for Diverse DNA Target Sites," *Science* 275:657-661 (1997);

Hamilton et al., "Comparison of the DNA Binding Characteristics of the Related Zinc Finger Proteins WT1 and EGR1," *Biochemistry* 37:2015-2058 (1998);

Hamilton et al., "High Affinity Binding Sites for the Wilms' Tumor Suppressor Protein WTI," *Nuc. Acids. Res.* 23(2):277-284 (1995);

Hanas et al., "Internal Deletion Mutants of *Xenopus* Transcription Factor IIIA," *Nuc. Acids. Res.* <u>17</u>(23):9861-9870 (1989);

Hayes et al., "Locations of Contacts Between Individual Zinc Fingers *Xenopus laevis* Transcription Factor IIIA and the Internal Control Region of a 5S RNA Gene," *Biochemistry* 31:11600-11605 (1992);

Heinzel et al., "A Complex containing N-CoR, MSin3 and Histone Deacetylese Medates Transcriptional Repression," *Nature* <u>387</u>:43-48 (1997);

Hirst et al., "Discrimination of DNA Response Elements for Thyroid Hormone and Estrogen is Dependent on Dimerization of Receptor DNA Binding Domains," *PNAS* 89:5527-5531 (1992);

Hoffman et al., "Structures of DNA-Binding Mutant Zinc Finger Domains: Implications for DNA Binding," *Protein Science* 2:951-965 (1993);

Imhof et al., "Transcriptional Regulation of the AP-Zalpha Promoter by BTEB-1 and AP-ZREP, a Novel WT-1/EGR-Related Zinc Finger Repressor," *Molecular and Cellular Biology* 19(1):194-204 (1999);

Isalan et al., "Synergy Between Adjacent Zinc Fingers in Sequence-Specific DNA Recognition," *PNAS* 94(11):5617-5621 (1997);

Isalan et al., "Comprehensive DNA Recognition Through Concerted Interactions from Adjacent Zinc Fingers," *Biochemistry* 37:12026-12033 (1998);

Jacobs, G.H., "Determination of the Base Recognition Positions of Zinc Fingers From Sequence Analysis," *EMBO J.* 11(12):4507-4517 (1992);

Jamieson et al. "A Zinc Finger Directory for High-Affinity DNA Recognition," *PNAS* 93:12834-12839 (1996);

Jamieson et al., "In Vitro Selection of Zinc Fingers with Altered DNA-Binding Specificity," *Biochemistry* 33:5689-5695 (1994);

Julian et al., "Replacement of His23 by Cys in a Zinc Finger of HIV-1NCp7 Led to a Change in 1H NMR-Derived 3D Structure and to a Loss of Biological Activity," *FEBS Letters* 331(1,2):43-48 (1993);

Kamiuchi et al., "New Multi Zinc Finger Protein: Biosynthetic Design and Characteristics of DNA Recognition," *Nucleic Acids Symposium Series* 37:153-154 (1997);

Kang et al., "Zinc Finger Proteins as Designer Transcription Factors, J. Biol. Chem. 275(12):8742-8748 (2000);

Kim et al., "Serine at Position 2 in the DNA Recognition Helix of a Cys2-His2 Zinc Finger Peptide is Not, in General, Responsible for Base Recognition," *J. Mol. Biol.* 252:1-5 (1995);

Kim et al., "Site-Specific Cleavage of DNA-RNA Hybrids by Zinc Finger/FokI Cleavage Domain Fusions," Gene 203:43-49 (1997);

Kim et al., "A 2.2 A° Resolution Crystal Structure of a Designed Zinc Finger Protein Bound to DNA," *Nat. Struct. Biol.* 3(11):940-945 (1996);

Kim et al., "Design of TATA Box-Binding Protein/Zinc Finger Fusions for Targeted Regulation of Gene Expression," *PNAS* 94:3616-3620 (1997);

Kim et al., "Hybrid Restriction Enzymes: Zinc Finger Fusions Fok I Cleavage Domain," PNAS 93:1156-1160 (1996);

Kim, J.S. and Pabo, C.O., "Getting a Handhold on DNA: Design of Poly-Zinc finger Proteins with Femtomolar Dissociation Constants," *Proc. Natl. Acad. Sci. U.S.A.* 95:2812-2817 (1998);

Kim, J.S. and Pabo, C.O., "Transcriptional Repression by Zinc Finger Peptides," *The Journal of Biological Chemistry* 272:29795-28000 (1997);

Kinzler et al., "The GLI Gene is Member of the Kruppel Family of Zinc Finger Proteins," Nature 332:371-374 (1988);

Kirwacki et al., "Sequence-Specific Recognition of DNA Zinc-Finger Peptides Derived From the Transcription Factor Sp1," *Proc. Natl. Acad. Sci. U.S.A.* 89:9859-9763 (1992);

Klug, A., "Gene Regulatory Proteins and Their Interaction with DNA," Ann. NY Acad. Sci. 758:143-160 (1995);

Klug et al., "Protein Motifs 5: Zinc Fingers," FASEB J. 9:597-604 (1995);

Klug, "Zinc Finger Peptides for the Regulation of Gene Expression," J. Mol. Biol. 293:215-218 (1999);

Kothekar, "Computer Simulation of Zinc Finger Month from Cellular Nucleic Acid Binding Proteins and Their Interaction with Consensus DNA Sequences," *FEB Letters* 274(1,2):217-222 (1990);

Kulda et al., "The Regulatory Gene areA Mediating Nitrogen Metabolite R in Aspergillus nidulans Mutations Affecting Specificity of Gene Activation Alter a Loop Residue of Putative Zinc Finger," EMBO J. 9(5):1355-1364 (1990);

Laird-Offringa et al., "RNA-Binding Proteins Tamed," Nat. Structural Biol. 5(8):665-668 (1998);

Liu et al., "Regulation of an Endogenous Locus Using a Panel of Designed Zinc Finger Proteins Targeted to Accessible Chromatin Regions: Activation of Vascular Endothelial Growth Factor A," *Journal of Biological Chemistry* 276(14):11323-11334 (2001);

Liu et al., "Design of Polydactyl Zinc-Finger Proteins for Unique Addressing Within Complex Genomes," *Proc. Natl. Acad. Sci. U.S.A.* <u>95</u>:5525-5530 (1997);

Liu et al., "Transcription Factor EGR-1 Suppresses the Growth and Transformation of Human HT-1080 Fibrosarcoma Cells by Induction of Transforming Growth Factor Beta 1," Proceedings of the National Academy of Science, Washington 93(21):11831-11836 (1996);

Mandel-Gutfreund et al., "Quantitative Parameters for Amino Acid-Base Interaction: Implication for Predication of Protein-DNA Binding Sites," *Nuc. Acids Res.* 26(10):2306-2312

(1998);

1 - 4 - 1 - 4 - 3

Margolin et al., "Kruppel-Associated Boxes are Potent Transcriptional Repression Domains," *PNAS* 91:4509-4513 (1994);

Mizushima et al., "pEF-BOS, a Powerful Mammilian Expression Vector," *Nuc. Acids. Res.* 18(17):5322 (1990);

Nakagama et al., "Sequence and Structural Requirements for High-Affinity DNA Binding by the WT1 Gene Product," *Molecular and Cellular Biology* 15(3):1489-1498 (1997);

Atty Dkt No. 8325-0002.01 USSN: 09/897,844

PATENT

Nardelli et al., "Zinc Finger-DNA Recognition: Analysis of Base Specificity by Site-Directed Mutagenesis," *Nucleic Acids Research* 20(16):4137-4144 (1992);

Nardelli et al., "Base Sequence Discrimination by Zinc-Finger DNA-Binding Domians," Nature 349:175-178 (1991);

Nekludova et al., "Distinctive DNA Conformation With Enlarged Major Groove is Found in Zn-Finger-DNA and Other Protein-DNA Complexes," *PNAS* 91:6948-6952 (1994);

Orkin et al., "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy," (1995);

Pabo et al., "Systematic Analysis of Possible Hydrogen Bonds between Amino Acid Side Chains and B-form DNA," J. Biomolecular Struct. Dynamic 1:1039-1049 (1983);

Pabo et al., "Protein-DNA Recognition," Ann. Rev. Biochem. 53:293-321 (1984);

Pabo, C. O., "Transcription Factors: Structural Families and Principals of DNA

Recognition," Ann. Rev. Biochem. 61:1053-1095 (1992);

 $\frac{1}{1} = \frac{1}{3} \cdot \frac{1}{1} \cdot \frac{1}{2} \cdot \frac{1}{2} \cdot \frac{1}{2}$

Pavletich et al., "Crystal Structure of a Five-Finger GLI-DNA Complex: New Perspectives on Zinc Fingers," *Science*, <u>261</u>:1701-1707 (1993);

Pavletich et al., "Zinc Finger-DNA Recognition: Crystal Structure of a Zif268-DNA Complex at 2.1 A," Science <u>252:</u>809-817 (1991);

Pengue et al., "Repression of Transcriptional Activity at a Distance by the Evolutionarily Conserved KRAB Domain Present in a Subfamily of Zinc Finger Proteins," *Nuc. Acids Res.* 22(15):2908-2914 (1994);

Pengue et al., "Transcriptional Silencing of Human Immunodeficiency Virus Type I Long Terminal Repeat-Driven Gene Expression by the Kruppel-Associated Box Repressor Domain Targeted to the Transactivating Response Element," *J. Virology* 69(10):6577-6580 (1995);.

Pengue et al., "Kruppel-Associated Box-Mediated Repression of RNA Polymerase 11 Promoters is Influenced by the Arrangement of Basal Promoter Elements," PNAS <u>93</u>:1015-1020 (1996);

Pomerantz et al., "Analysis of Homeodomain Function by Structure-Based Design of a Transcription Factor," PNAS 92:9752-9756 (1995);

Pomerantz et al., "Structure-Based Design of Transcription Factors," Science 267:93-96 (1995);

Atty Dkt No. 8325-0002.01 USSN: 09/897,844

PATENT

Pomerantz et al., "Structure-Based Design of a Dimeric Zinc Finger Protein," Biochemistry 37(4):965-970 (1998);

1 1 1

Qian et al., "Two-Dimensional NMR Studies of the Zinc Finger Motif:. Solution Structures and Dynamics of Mutant ZFY Domains Containing Aromatic Substitutions in the Hydrophobic Core," Biochemistry 31:7463-7476 (1992);

Quigley et al., "Complete Androgen Insensitivity Due to Deletion of Exon C of the Androgen Receptor Gene Highlights the Functional Importance of the Second Zinc Finger of the Androgen Receptor in Vivo," Molecular Endocrinology 6(7):1103-1112 (1992);

Rauscher et al., "Binding of the Wilms' Tumor Locus Zinc Finger Protein to the EGR-I Consensus Sequence," Science 250:1259-1262 (1990);

Ray et al., "Repressor to Activator Switch by Mutations in the First Zn Finger of the Glucocorticoid Receptor: Is Direct DNA Binding Necessary?," PNAS 88:7086-7090 (1991);

Rebar et al., "Phage Display Methods for Selecting Zinc Finger Proteins with Novel DNA-Binding Specificities," Methods in Enzymology 267:129-149 (1996);

Rebar et al., "Zinc Finger Phage: Affinity Selection of Fingers With New DNA-Binding Specifities," Science 263:671-673 (1994);

Reith et al., "Cloning of the Major Histocompatibility Complex Class II Promoter Binding Protein Affected in a Hereditary Defect in Class II Gene Regulation," PNAS 86:4200-4204 (1989);

Rhodes et al., "Zinc Fingers: They Play a Key Part in Regulating the Activity of Genes in Many Species, From Yeast to Humans. Fewer Than 10 Years Ago No One Knew They Existed." Scientific American <u>268</u>:56-65 (1993);

Rice et al., "Inhibitors of HIV Nucleocapsid Protein Zinc Fingers as Candidates for the Treatment of AIDS," Science. 270:1194-1197 (1995);

Rivera et al., "A Humanized System for Pharmacologic Control of Gene Expression," Nature Medicine <u>2</u>(9):10281032 (1996);

Rollins et al., "Role of TFIIIA Zinc Fingers In vivo: Analysis of Single-Finger Function in Developing Xenopus Embryos," Molecular Cellular Biology 13(8):4776-4783 (1993);

Saleh et al., "A Novel Zinc Finger Gene on Human Chromosome 1 qter That is Alternatively Spliced in Human Tissues and Cell Lines," *American Journal of Human Genetics* 52:192-203 (1993);

Shi et al., "Specific DNA-RNA Hybrid Binding by Zinc Finger Proteins," Science 268:282-284 (1995);

1, , 1,

Shi et al., "DNA Unwinding Induced by Zinc Finger Protein Binding," *Biochemistry* 35:3845-3848 (1996);

Shi et al., "A Direct Comparison of the Properties of Nnatural and Designed Finger Proteins," *Chem. & Biol.* 2(2):83-89 (1995);

Singh et al., "Molecular Cloning of an Enhancer Binding Protein: Isolation by Screening of an Expression Library with a Recognition Site DNA," Cell <u>52</u>:415-423 (1988);

Skerka et al., "Coordinate Expression and Distinct DNA-Binding Characteristics of the

Four EGR-Zinc Finger Proteins in Jurkat T Lymphocytes," *Immunobiology* 198:179-191 (1997); South et al., "The Nucleocapsid Protein Isolated from HIV-1 Particles Binds Zinc and Forms Retroviral-Type Zinc Fingers," *Biochemistry* 29:7786-7789 (1990);

Spengler et al., "Regulation of Apoptosis and Cell Cycle Arrest by ZZC1, A Novel Zinc finger Protein Expressed in the Pituitary Gland and the Brain," *EMBO Journal 6B, Oxford University Press, Surrey* 16(10):2814-2825 (1997);

Suzuki et al., "Stereochemical Basis of DNA Recognition by Zn Fingers," *Nuc. Acids Res.* 22(16):3397-3405 (1994);

Suzuki et al. "DNA Recognition Code of Transcription Factors in the Helix-turn-Helix,

Probe Helix, Hormone Receptor, and Zinc Finger Families," *PNAS* 91:12357-12361 (1994); Swimoff et al., "DNA-Binding Specificity of NGFI-A and Related Zinc Finger Transcription Factors," *Mol. Cell. Biol.* 15(4):2275-2287 (1995);

Taylor et al., "Designing Zinc-Finger ADRI Mutants with Altered Specificity of DNA Binding to T in UASI Sequences," *Biochemistry* 34:3222-3230 (1995);

Thiesen et al., "Determination of DNA Binding Specificities of Mutated Zinc Finger Domains," FEBS Letters <u>283(1):23-26 (1991);</u>

Thiesen et al., "Amino Acid Substitutions in the SP1 Zinc Finger Domain Alter the DNA Binding Affinity to Cognate SP1 Target Site," *Biochem. Biophys. Res. Communications* 175(1):333-338 (1991);

Thiesen, H. J., "From Repression Domains to Designer Zinc Finger Proteins: A Novel Strategy for Intracellular Immunization Against HIV," *Gene Expression* 5:229-243 (1996);

Thukral et al., "Localization of a Minimal Binding Domain and Activation Regions in Yeast Regulatory Protein ADRI1," Molecular Cellular Biology 9(6):2360-2369 (1989);

Thukral et al., "Two Monomers of Yeast Transcription Factor ADR1 Bind a Paldromic Sequence Symmetrically to Activate *ADH2* Expression," *Molecular Cellular Biol.* <u>11</u>(3):1566-1577 (1991);

Thurkral et al., "Alanine Scanning Site-Directed Mutagenesis of the Zinc Fingers of Transcription Factor ADR1: Residues that Contact DNA and that Transactivate," *PNAS* <u>88</u>:9188-9192 (1999 1), + correction page;

Thukral et al., "Mutations in the Zinc Fingers of ADR1 That Change the Specificity of DNA Binding and Transactivation," *Mol. Cell Biol.* 12(6):2794-2792 (1992);

Vortkamp et al., "Identification of Optimized Target Sequences for the GL13 Zinc Finger Protein," DNA Cell Biol. 14(7):629-634 (1995);

Wang et al., "Dimerization of Zinc Fingers Mediated by Peptides Evolved *In Vitro* From Random Sequences," *Proc. Natl. Acad. Sci. U.S.A.* <u>96</u>:9568-9573 (1999);

Webster et al., "Conversion of the E1A Cys4 Zinc Finger to a Nonfunctional His2, Cys2 Zinc Finger by a Single Point Mutation," *PNAS* 88:9989-9993 (1991);

Whyatt et al., "The Two Zinc Finger-Like Domains of GATA-1 Have Different DNA Binding Specificities," *EMBO J.* 12(13):4993-5005 (1993);

Wilson et al., "In Vivo Mutational Analysis of the NGFI-A Zinc Fingers," J. Biol. Chem. 267(6):3718-3724 (1992);

Witzgall et al., The Kruppel-Associated Box-A (KRAB-A) Domain of Zinc Finger Proteins Mediates Transcriptional Repression" *PNAS* 91:4514-4518 (1994);

Wright et al., "Expression of a Zinc Finger Gene in HTLV-1 and HTLV-II Transformed Cells," Science 248:588-591 (1990);

Wolfe et al., "Analysis of Zinc Fingers Optimized *Via* Phage Display: Evaluating the Utility of a Recognition Code," *J. Mol. Biol.* 285:1917-1934 (1999);

Wu et al., "Building Zinc Fingers by Selection: Toward a Therapeutic Application," *Proc. Natl. Acad. Sci. U.S.A.* 92:344-348 (1995);

Yang et al., "Surface Plasmon Resonance Based Kinetic Studies of Zinf Finger-DNA Interaction," *J. Immunol. Methods* 183:175-185 (1995);

Yu et al., "A Hairpin Ribozyme Inhibits Expression of Diverse Strains of Human Immunodeficiency Virus Type 1," PNAS 90:6340-6344 (1993);

Zhang et al., "Synthetic Zinc Finger Transcription Factor Action at an Endogenous Chromosomal Site. Activation of the Human Erythropoietin Gene," *Journal of Biological Chemistry* 275(43):33850-33860 (2000); and

Search of Swissprot. Database Performed CA August 2000.

This Information Disclosure Statement is not to be construed as a representation that: (i) additional information material to the examination of this application does not exist; (ii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iii) the above information constitutes prior art to the subject invention.

Respectfully submitted,

Date: Nov 14, 200/

Rv

Dahna S. Pasternak Registration No. 41,411

ROBINS & PASTERNAK LLP 90 Middlefield Road, Suite 200 Menlo Park, CA 94025

Telephone: (650) 325-7812

Fax: (650) 325-7823